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EXAMINER	
CELSA, BENNETT M	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 01/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/291,426	JAMES ET AL.	
	Examiner	Art Unit	
	Bennett Celsa	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-12,14-17 and 21-28* is/are pending in the application.

4a) Of the above claim(s) *6-8,11,12,15,16,22,25 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5, 9, 10, 14, 17, 21, 23, 24, 26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

Applicant's amendment dated 10/2/03 is hereby acknowledged.

Status of the Claims

Claims 1, 5-12, 14-17 and 21-28 are currently pending.

Claims 6-8, 11-12, 15, 16, 22, 25 and 28 are withdrawn from consideration as being directed to a nonelected invention.

Claims 1, 5, 9, 10, 14, 17, 21, 23, 24, 26 and 27 are under consideration

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restriction

2. Applicant's election, without traverse, of Group I (claims 1-27) and species election in paper no. 7 and 10 in response to the restriction/election requirement in paper no. 5 is again acknowledged. In papers no. 7 and 10 applicant elected:

a. Group I, claims 1-27;

b. The species of claims 5, 14, 17 and 21;

c. Elected a compound of the structure depicted in claim 21:

wherein b is 1; R1 is (CH2)a, wherein a is 2, in which the R1 linking moiety on the left side of the first monomeric structure is attached to the left side of the benzene ring para to the hydroxy group attached to the aforementioned ring and the (CH2)b moiety on the right side of the first monomeric structure is attached to the right side of the benzene ring.

d. The species of claim 19, wherein:

1. The second monomer series is carboxylic acids;

[2. The third monomer series is ethylene oxide; embodiment cancelled by applicant]

e. The species of claim 28, wherein copolymers are further modified by crosslinking.

3. This application contains claims 6-8, 11-12, 15, 16, 22, 25 and 28 drawn to a nonelected invention. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Withdrawn Objection (s) and/or Rejection (s)

Applicant's amendment and accompanying argument has overcome the indefinite rejection (items A. and B.) of claims 1-3, 5, 9, 10, 14, 17-18, 20, 21, 23, 24, 26 and 27 presented in the prior office action.

Applicant's amendment and accompanying argument has overcome the new matter rejection of claims 1-3, 5, 9, 10, 14, 17-18, 20, 21, 23, 24, 26 and 27 presented in the prior office action.

Applicant's amendment and accompanying argument has overcome the written description rejection of claims 1-3, 5, 9, 10, 14, 17-18, 20, 21, 23, 24, 26 and 27 presented in the prior office action.

Applicant's amendment and accompanying argument has overcome the enablement rejection of claims 1-3, 5, 9, 10, 14, 17-18, 20, 21, 23, 24, 26 and 27 presented in the prior office action.

Applicant's argument has overcome the anticipation rejection of claims 1-3, 5, 9, 10, 14, 17-18, 20, 21, 23, 24, 26 and 27 under 35 U.S.C. 102(a) as being anticipated or

in the alternative as obvious over Brocchini et al. JACS Vol. 119 (5/14/97) pages 4553-4554.

Outstanding Objection (s) and/or Rejection (s)

4. Claims 1, 5, 9, 10, 14, 17, 21, 23, 24, 26 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by, or in the alternative as obvious over Fiordeliso et al. J.Biomater. Sci. Polyer Edn. Vol. 5, No. 6 pages 497-510 (1994) alone, or if necessary, further in view of Brocchini et al. JACS (5/14/97) pages 4553-4554 for demonstrating INHERENCY. .

Present claims 1, 5, 9, 10, 14, 17, 21, 23, 24, 26 and 27 are drawn to "product by process claims" which define the product by its method of making. See MPEP 2113directed to " Product by Process Claims " . Even though product - by process claims are limited by and defined by the process, determination of patentability is *based on the product itself.* The patentability of a product does not depend on its method of production. If the product in the product - by - process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe* , 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). Once the Examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. *In re Marosi*, 218 USPQ 289, 292 (Fed. Cir. 1983).When the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product - by - process claim, a rejection based

alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown* , 173 USPQ 685, 688 (CCPA 1972).

In the present case, the product is drawn to a library of "strictly alternating A-B type copolymers" comprising " a number of homologously bivariant copolymers sufficient to incrementally establish quantitative structure-property correlations" which is formed from parallel polymerization of monomers. In a specific embodiment (e.g. claims 21, 23, 24 and 26) the copolymer library is formed by polymerizing:

a. 1st monomer of a homologous series of varying monomers with polymerizable carboxylic groups:

with a

b. 2nd monomer of a homologous series of varying monomers with polymerizable hydroxyl groups.

wherein the 1st monomer is preferably a dicarboxylic acid and and the 2nd monomer is a diphenol resulting in a library of polyarylates;

resulting in "polymers of sufficiently similar molecular weights and polydispersities to establish meaningful (quantitative) library-wide stucture property correlations".

Fiordeliso et al. teach a library of five *separately (co) polymerized* (E.g. condensed, in liquid solution) polyarylates which were synthesized from "homologous" "diacid" monomer component and a "homologous" diphenol monomer components (e.g. see Figures 1 and 2). It is noted that the reference teaching of a *"library"* (e.g. a

collection) of five distinct polyarylates copolymers regardless of the means of syntheses (separately or otherwise) meets the presently claimed product-by-process claims since this type of claim is viewed by the PTO as a product claim.In any event the reference does teach the use of method steps within the scope of the presently claimed invention .

Further, the reference teaches that the polyarylates can be "further modified" by "chemical reactions" since the polymers "degraded" (e.g. underwent a "chemical reaction") under physiological conditions (e.g. see Abstract); thus meeting present claims 9 & 27.

The Fiordeliso et al. Copolymer library members possess "similar molecular weight and polydispersities" (e.g. see Fig. 3; table 2) which establishes "meaningful library-wide structure property correlations" as indicated by the correlation of various structure properties (e.g.. thermochemical; hyrdolytic degradation; release studies) to the various reference copolymer library members (e.g. see pages 504-509; tables and figures).

Additionally, the Fiordeliso et al. Reference suggests the syntheses of larger libraries including:

a. Different diphenols components having pendent chains of ethyl to octyl (e.g. y is 2-8); and

b. Different diacid compoents having 2-8 flexible -CH2- units in the diacid polymer backbone.

E.g. See page 499 figure 2 and first full paragraph.

Accordingly, the Fiordello reference discloses and sugest polyarylate libraries of from 5 to 49 or more (e.g. 7 (diphenols)x7(diacids)) derived from "homologous"(e.g. differing by -CH2-) tyrosine diphenols and "homologous" (e.g. differing by -CH2-) diacids which would represent a "number of homologously bivariant copolymers sufficient to incrementally establish quantitative structure-property correlations" since the present claims are not limited to a library number of compounds and additionally as illustrated by the screening of the Fiordello library compounds for various properties e.g. polymer glass transition temperatures; dye release etc.

Additionally, the Fiordello reference INHERENLY teaches "the making of 'strictly alternating' A-B type copolymers within the scope of the presently claimed invention since the Fiordello reference teaches : polymerizing

a. the 1st monomer contains a reactive group for attachment of a series of 'pendent chains' (e.g. "R" variable); and

b. the 2nd monomer allows for systematic variations in the polymer backbone structure" (e.g. the "Y" variable); (e.g. the "homologous variations of said 1st and 2nd momoner series ... have a different influence on polymer properties ..." and

"since all polymers were derived from very similar monomers, they could be prepared under identical reaction conditions ... " . See page Brocchin et al. at 4553, especially left column.

Thus the reference library is clearly within the scope of the presently claimed invention which renders properties (not explicitly taught by the reference) of such

compounds presently recited inherent (e.g. "sufficiently high molecular weight"; "similar polydispersity" etc) with intended use limitations (e.g. in compound/composition claims) not being afforded patentable weight (e.g. "incrementally establish quantitative structure property correlations").

Discussion

Applicant's arguments directed to the above rejection were considered but deemed nonpersuasive for the following reasons. Initially, it is noted that above rejection was modified in response to applicant's amendment.

Applicant argues that the Brocchini et al. reference is not prior art and the use of this reference by the Examiner "is a classic example of the impermissible hindsight reconstruction ...". This argument is not persuasive.

Applicant's argument fails to address the use of the Brocchini document in the rejection above, not as a reference by the Examiner as alleged by applicant, but for the purposes of providing extrinsic evidence of inherency, which does not constitute impermissible hindsight. See MPEP 2131.01(d) which permits the citation of references or any extrinsic evidence in order to show that a characteristic not disclosed in a reference is inherent.

Applicant argues that the Fiordello reference neither teaches the conditions nor the requisite number of library *polymers* within which meaningful relevant library wide-structure property correlations can be made. Applicant further argues that any suggestion by Fiordello to expand the library does not take into account how to control

the reaction conditions to ensure an expanded library of polymers that are sufficiently similar to permit relevant structure-property comparisons over the entire library.

This argument is not persuasive for the following reasons.

The Fiordello reference clearly provides reaction conditions for syntheses of "homologously bivariant copolymers" possessing similar weights and/or dispersities in a sufficient manner to establish meaningful quantitative structure-property correlations as demonstrated in the Fiordello examples. See above rejection citing tables and figures regarding mw/dispesities and structure/function correlation (e.g. measuring thermal and drug release properties). Applicant has failed to provide any scientific rationale to the contrary. Applicant's arguments addressing the number of Fiordello compounds synthesized and tested (e.g. "limited number of polymer structures") as contrasted with "an expanded library of polymers" is not convincing since applicant's claims are not so limited (e.g. by number of compounds). Accordingly, the Fiordello reference teaching of making "meaningful" "quantitative structure-property correlations" for the Fiordello library members and its explicit motivation to increase the size of the Fiordello libraries anticipates or in the alternative renders obvious the presently claimed invention.

Accordingly, the above rejection, as modified, is hereby maintained.

5. Claims 1, 5, 9, 10, 14, 17, 21, 23, 24, 26 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by, or in the alternative as obvious over Kohn et al. US Pat. No. 5,216,115 (6/93).

Present claims 1, 5, 9, 10, 14, 17, 21, 23, 24, 26 and 27 are drawn to "product by process claims" which define the product by its method of making. See MPEP 2113directed to " Product by Process Claims " . Even though product - by process claims are limited by and defined by the process, determination of patentability is *based on the product itself.* The patentability of a product does not depend on its method of production. If the product in the product - by - process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe* , 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). Once the Examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. *In re Marosi*, 218 USPQ 289, 292 (Fed. Cir. 1983).When the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product - by - process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown* , 173 USPQ 685, 688 (CCPA 1972).

In the present case, the product is drawn to a library of "strictly alternating A-B type copolymers" comprising " a number of homologously bivariant copolymers sufficient to incrementally establish quantitative structure-property correlations" which is

formed from parallel polymerization of monomers. In a specific embodiment (e.g. claims 21, 23, 24 and 26) the copolymer library is formed by polymerizing:

a. 1st monomer of a homologous series of varying monomers with polymerizable carboxylic groups:

with a

b. 2nd monomer of a homologous series of varying monomers with polymerizable hydroxyl groups.

wherein the 1st monomer is preferably a dicarboxylic acid and and the 2nd monomer is a diphenol resulting in a library of polyarylates;

resulting in "polymers of sufficiently similar molecular weights and polydispersities to establish meaningful (quantitative) library-wide stucture property correlations".

Kohn et al. teaches a collection (e.g. library) of aliphatic/aromatic polyarylates having repeating structural units (e.g. see col. 4 and formula 1) which represents a collection of "strictly alternating A-B type copolymers" within the scope of the presently claimed invention. The copolymers represent "a number of homologously bivariant copolymers" within the scope of the presently claimed invention (e.g. see col. 4-5: formula I where X is H; Y is a pendent group; and R is as defined in column 5, including unsubstitued alkyl) which contain a varying monomer backbone (e.g. R variable of dicarboxylic acid) and a varying substituent group (e.g. the Y pendent group of the dihydroxy tyrosine derived monomer). Thus the reference library is clearly within the scope of the presently claimed invention which renders properties of such compounds presently recited inherent (e.g. "sufficiently high molecular weight"; "similar

polydispersity" etc) with intended use limitations (e.g. in compound/composition claims) not being afforded patentable weight (e.g. "incrementally establish quantitative structure property correlations"). In any event it is further noted that the Kohn reference teaches methods of syntheses, library compound molecular weights and screening of the compound libraries for librarywide "meaningful" quantitative structure property correlations" which are within the scope of the presently claimed invention e.g. see examples; particularly examples and col. 12-13.

Discussion

Applicant's arguments directed to the above rejection were considered but deemed nonpersuasive for the following reasons. Initially, it is noted that above rejection was modified in response to applicant's amendment.

Applicant argues that the Kohno reference neither teaches the conditions nor the requisite number of library *polymers* within which meaningful relevant library wide-structure property correlations can be made. Applicant further argues that any suggestion by Kohn to expand the library does not take into account how to control the reaction conditions to ensure an expanded library of polymers that are sufficiently similar to permit relevant structure-property comparisons over the entire library.

This argument is not persuasive for the following reasons.

The Kohn reference clearly provides reaction conditions for syntheses of "homologously bivariant copolymers" possessing similar weights and/or dispersities in a sufficient manner to establish meaningful quantitative structure-property correlations as demonstrated in the Kohn examples. See above rejection citing, examples and relevant

tables and figures regarding mw/dispesities and structure/function correlation (e.g. measuring thermal and drug release properties). Applicant has failed to provide any scientific rationale to the contrary. Applicant's arguments addressing the number of Kohn compounds synthesized and tested (e.g. "limited number of polymer structures") as contrasted with "an expanded library of polymers" is not convincing since applicant's claims are not so limited (e.g. by number of compounds). Accordingly, the Kohn reference teaching of making "meaningful" "quantitative structure-property correlations" for the Kohn library members and its motivation to increase the size of the Kohn libraries anticipates or in the alternative renders obvious the presently claimed invention.

Accordingly, the above rejection, as modified, is hereby maintained

6. Claims 1, 5, 9, 10, 14, 17, 21, 23, 24, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kohn et al., U.S. Patent No.5,216,115 A, Filed: August 13, 1992, Issued: Junel, 1993, Gordon et al. (J. Med. Chem., 1994, Vol. 37, No. 10, 1385-1401) and Still et al., U.S. Patent N0.5,565,324, Filed: April 13, 1994, Issued: October 15, 1996.

Kohn et al. teaches: (1) polyacrylates and methods for the synthesis of bioerodible polyarylates derived from biocompatible dicarboxylic acids and natural amino acid-derived diphenol starting materials; (2) wherein a polymerization process includes the reaction of diphenol compounds (formed from amino acid-derived monomers) are then reacted with aliphatic or aromatic dicarboxylic acids in a carbodiimide-mediated direct polyesteritication using DPTS as a

catalyst to form aliphatic or aromatic polyarylates recovering the resulting polyarylate. (3) wherein said bioerodible polyarylates derived from the natural amino acid L-tyrosine derived diphenols and biocompatible aromatic and aliphatic dicarboxylic acids; (4) wherein said polyarylates, include polymers having pendant side chains on each repeating unit (i.e., said structural feature represents a further degree of freedom in the design of polyarylates and can be used to modify the overall physicomechanical properties of the polymer without changing the polymer backbone structure); and alternatively, the pendent side chains can be used to crosslink the polymer chains to form a polymeric matrix into which a biologically or pharmacologically active material can be physically imbedded or dispersed; (5) wherein said aliphatic and/or aromatic dicarboxylic acids, include substituted- and unsubstituted alkyl or alkylaryl groups containing up to l8 carbon atoms and preferred aliphatic dicarboxylic acid starting materials therefore which include the intermediate dicarboxylic acids of the cellular respiration pathway known as the Krebs Cycle (i.e., these dicarboxylic acids include alpha-ketoglutaric acid, succinic acid, fumaric acid, malic acid and oxaloacetic acid, etc.) and (6) wherein the products form nontoxic bioerodible and biodegradable products and are usable as degradable, medical implant materials., i.e., molded articles prepared from the polyarylates are useful, inter alia, as degradable biomaterials for medical implant applications: for use as vascular graphs and stents, bone plates, sutures, implantable sensors, barriers for surgical adhesion prevention, implantable drug delivery devices and other therapeutic aids and articles which decompose harmlessly within a known period of time.

Accordingly, Kohn et al. teaches a collection (e.g. library) of aliphatic/aromatic polyarylates having repeating structural units (e.g. see col. 4 and formula 1) which represents a collection of "strictly alternating A-B type copolymers" within the scope of the presently claimed invention. The copolymers represent "a number of homologously bivariant copolymers" within the scope of the presently claimed invention (e.g. see col. 4-5: formula I where X is H; Y is a pendent group; and R is as defined in column 5, including unsubstitued alkyl) which contain a varying monomer backbone (e.g. R variable of dicarboxylic acid) and a varying substituent group (e.g. the Y pendent group of the dihydroxy tyrosine derived monomer). Thus the reference library is clearly within the scope of the presently claimed invention which renders properties of such compounds presently recited inherent (e.g. "sufficiently high molecular weight"; "similar polydispersity" etc) with intended use limitations (e.g. in compound/composition claims) not being afforded patentable weight (e.g. "incrementally establish quantitative structure property correlations"). In any event it is further noted that the Kohn reference teaches methods of syntheses, library compound molecular weights and screening of the compound libraries for librarywide "meaningful" quantitative structure property correlations" which are within the scope of the presently claimed invention e.g. see examples; particularly examples and col. 12-13.

In view of the above, the aforementioned Kohn et al. U.S. Patent differs (if at all) from the claimed invention in that it does not teach the synthesis of multi-dimensional arrays of the aforementioned polymers by using the synthetic methods of preparation as defned above.

However, Gordon et al. teaches: (1) the application of known pharmacophores amenable to assembly via combinatorial methods to form libraries, arrays (i.e., compositions of two or more) with known synthetic organic reaction processes for the synthesis of identised target or biological compounds) and/or generation of combinatorial libraries', and (2) the construction and or use of large compound libraries for uses such as biological assays or screening.

Gordon et al. Further teaches (1) "when small-molecule leads for a target have been previously defined the notion-of searching-for more potent deivatives among libraries combinatorially enriched in specific pharmacophore analogs is an obvious tactic to pursue (see, page 12591, col. 2, lines 18-21)", (2) the applicability of a "spectrum of molecular diversity" strategy in the generation of a library, array or combinatorial library, array, etc. comprised of a few to many molecules (such an approach approximates the number of molecules of in a given library based upon molecule type, i.e., recombinant or multi-peptides, encoded, non-encoded synthetic or recursively factored compounds, etc. (see, page 1397, Figure 19 and lines 19 to 21), (3) that "a key aspect in the successful application of combinatorial technologies to drug discovery is the requirement for having a closely linked, coordinates process for the integration of synthesis and screening" (see page 1397, col. 2, lines 7-12),. and (4) successful application of "molecular diversity" strategies to develop methods of synthesis and screening of compounds and/or combinatorial libraries are possible when a conventional organic target compounds with a known biological pharmacophore activity is identified with a known synthetic route or reaction sequence; such methods of

synthesis and screening combinatorial libraries, conducting a synthetic reaction by immobilization of reactant compounds, receptors, etc. via spacers or linkers (i.e., e.g., such as polyoxyethylene) spacer moiety, see col. 2, line 30,. also see Still et al. teaches the a general list and the use of conventional linkers with bi-functionality, whereby the resin and building blocks can be attached to either end of the linker, which include alkyl diols, see, col. 12, line 56-60, Linker F; to conventionally known solid supports (i.e., e.g., such as, microtiter plates, Merrifield –resins, see-col 2, page 1240, lines 24-36, Tentagel-resin beads of 90 um diameter, see-page 1246, line 26-35,. polyacrylamide and halogenated resins, see page 1246, col. 2, lines 23-26, which read on claims 17 and 23 of the claimed invention), beads, polymeric resins, microtiter wells or chromatography supports followed by the capture of complexes (see generally for examples of resins, linkers described therein and page 1393, col. I , lines 31-43 to col. 2, lines 1-18).

A person of ordinary skill in the art would have been motivated to make and screen novel co-polymer arrays of poly acrylates, prepared by the condensation of tyrosine derived diphenol compounds and different monomers, because such polymer products form nontoxic bioerodible and biodegradable products and are usable as degradable, medical implant materials with practical medicinal applications as taught by Kohn et al.

Additionally, the Still '324 reference teaches that combinatorial syntheses can be performed, at the option of the practitioner, as a matter of design choice, in either the same vessel or in different vessels (e.g. separate syntheses e.g. an array format): " In

carrying out the syntheses ... One can use microtiter well plates, individual containers, columns, gels, Terasaki plates, flasks, Merifield syntheses vessels, etc. (E.g. see col. 15, lines 7-20: see also col. 15, lines 32-col. 16, line 21). Accordingly, making the library in one vessel or in separate vessels is an obvious design choice to one of ordinary skill in the art at the time of applicant's invention.

In light of foregoing, a person of ordinary skill in the art would have a reasonable expectation of success in synthesizing co-polymer arrays of polyacrylates, prepared by the condensation of tyrosine derived diphenol compounds and different monomers, such as dicyanates and corresponding derivative compounds, because (1) Kohn et al. teaches the synthetic methods for the preparation of the aforementioned polymers are pharmacores with biological utility and a known synthetic preparation route; and (2) Gorden et al. teaches that "molecular diversity" strategies successfully are applied to known conventional organic target compounds with biological pharmacore utility, a known synthetic route wherein such strategies may be achieved to produce arrays.

It would have been prima facie obvious to a persion of ordinary skill in the art at the time of applicant's invention was made to modify the teachings of Kohn et al. with the teachings of Gordon et al. to synthesize co-polymer arrays, libraries, etc. and screen or assay those arrays and/or libraries.

Discussion

Applicant's arguments directed to the above obviousness rejection were considered but deemed nonpersuasive for the following reasons. Initially, it is noted that above rejection was modified in response to applicant's amendment.

Applicant argues that "One of ordinary skill in the polymer art recognizes that the presently claimed library of polymers with similar molecular weights and polydispersities cannot be made in a single pot process" since "This results in an inseparable mixture from which individual polymer species cannot be separated for the determination of structure-property correlations." This argument is not persuasive for several reasons.

Initially, it is noted that applicant fails to indicate what reference teaching is being referred to.

First, even if applicant's argument were agreed upon by the Examiner (which it is not), applicant has overlooked the fact that the claims are drawn to a product-by-process claims. Accordingly, the Examiner would argue that a single pot process would result in "A copolymer library of different copolymers" within the scope of the presently claimed invention, irrespective of whether the syntheses occurred in a single vessel or different vessels since the references (e.g. the Kohn patent references) polymerize monomer units within the scope of the presently claimed invention.

Secondly, to the extent that applicant is referring to the teaching of the Gordon reference, applicant's interpretation of the Gordon et al. reference appears to be misguided in several respects. The Gordon et al. reference, taken as a whole, suggests the applicability of "Combinatorial Technologies" to drug discovery *without limitation of the strategy employed.* The Examiner has not been able to locate a Gordon reference teaching that suggests only the use of a "single vessel" combinatorial syntheses to the exclusion of the parallel techniques. In fact the Gordon et al. reference appears to strongly *teach toward* performing parallel/simultaneous array (e.g. separate

reaction vessels) syntheses. E.g. see pages 1391-1393 (e.g. page 1392, left column, first line e.g. " on a solid support in an **array format**". Additionally, the author's biography (on the first page of the article, left column) describes one of the authors as "Stephen P.A. Fodor" who together with his colleagues "led the development of new technologies, *merging photolithography with combinatorial solid-phase chemistry.* As recognized by those of ordinary skill in the art, the Fodor et al. (E.g. from Affymetrix) photolithography/solid phase chemistry technique is a parallel syntheses technique **in an array format.**

Thirdly, in response to applicant's arguments against the Gordon et al. reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In this respect, the Still reference teaches that combinatorial syntheses can be performed, as a matter of design choice, in either one vessel , or separate vessels (e.g. array format).

Applicant further argues that "As recognized by one of ordinary skill in the polymer art, the presently claimed copolymer libraries do not encompass oligomers because the structural properties of oligomers do not resemble the structural properties of corresponding polymers. The terms are not interchangeable. No meaningful correlations to polymer structural properties for the library as a whole can be gleaned from polymer data." This argument is not persuasive for several reasons.

Initially, it is again noted that applicant fails to indicate what reference teaching is being referred to.

To the extent that applicant is referring to the Still reference teaching (e.g. applicant formerly argued that "Still et al. excludes polymers ... but instead is directed to "oligomers and synthetic non-repetitive organic molecules") it is respectfully noted that Applicant's interpretation of the Still et al. reference teaching is misguided since the Abstract clearly teaches that the Still et al. combinatorial method addresses "synthetic schemes" in which "*Various products* can be produced" ... *such as* oligomers and synthetic non-repetitive organic molecules. E.g see Still et al. Abstract. Accordingly, applicant's argument is misguided since the Still et al. combinatorial scheme addresses "Various products" and thus is not limited to any particular structure. Further, it would appear that the term "oligomer" would encompass the condensation of different monomer units as in the presently claimed invention. Thirdly, in response to applicant's arguments against the Still et al. reference individually, it is again noted that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this respect it is again further noted that the Still reference applies to the combinatorial syntheses of "Various products" in general, including oligomers, which should encompass combinatorial syntheses of polymers (e.g. via monomeric units) as presently claimed. Additionally, the Still reference teaches that combinatorial syntheses

can be performed, as a matter of design choice, in either one vessel , or separate vessels (e.g. array format).

Applicant in the future is encouraged to more specifically cite the portion of the article being referred to in argument(s) presented to the Examiner in order to facilitate the ability of the Examiner to address his/her concerns.

Applicant further argues that the "Gordon et al. and Still et al. do not teach or suggest the conditions necessary for a library of *polymers* to be produced within which relevant library wide-structure property correlations can be made" and "The Kohn et al. patents depict properties for a limited number of polymer structures". This argument is not persuasive for the following reasons.

The Kohn reference clearly provides reaction conditions for syntheses of "homologously bivariant copolymers" in a sufficient manner to establish meaningful quantitative structure-property correlations as demonstrated in the patent examples (e.g. measuring thermal and drug release properties). Forming parallel arrays as discussed in the secondary references utilizing the Kohn reference methods engenders more than a reasonable expectation of success. Applicant has failed to provide any scientific rationale to the contrary. Applicant's arguments addressing the number of Kohn compounds synthesized and tested (e.g. "limited number of polymer structures") as contrasted with "an expanded library of polymers" is not convincing since applicant's claims are not so limited (e.g. by number of compounds). Additionally, the Kohn reference teaching of making "meaningful" "quantitative structure-property correlations" for the Kohn library members taken alone or modification by size expansion of the

Kohn libraries (e.g. utilizing parallel syntheses i.e. arrays) as suggested by the secondary references would render obvious the presently claimed invention.

Thus, the above obviousness rejection, as modified, is hereby retained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bennett Celsa whose telephone number is 703-305-7556. The examiner can normally be reached on 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 703-306-3217. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bennett Celsa
Primary Examiner
Art Unit 1639

BC